

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100

1 GAATTCGGCGGAGCGCGAGAGAGAAAGTCACTTGCCCTGGCTCTACCTTGAAGTGGTTCAGGGTTGGGCGGAGAGTCGGGTGGGACCGAGATGC
101 AGCTCTATCCTGTGCCCTGTGTCGCAGCAGCCACGCGCTTCGCGTGTCTACTTGGCCTGTCCGCTGCCCTAATGAGCTCAGGTCTAGGCCGAG
201 CAGAGGGGCACCTGGTCGGACTCGGTGGCTCGGGCGGCCCGCCCTCCCGCCGCGGCGGCCCTTCTCGACGGCGCGGGCGGCCCTGCGG
301 GCGCGGGGCTGAAGCGGGAACCAACGACGGGCAGAGACCGGAGCCGGGAAGCCCTGGGCGGCCCGTGGAGGGCTATGGAGCAGCGCGCGGGCTGC
1 M E Q R P R G C
401 GCGCGGTGGCGGCGGCTCCTCTGCTGGTGGGCGGCCAGGGCGGCACTCGTAGCCCGCAGGTGTGACTGTGCCGTGACTTCCACAAGA
9 A A V A A L L V L L G A R A Q G G T R S P R C D C A G D F H K K
501 AGATTGGTCTGTTTGTGCAGAGGCTGCCAGCGGGCACTACCTGAAGCCCTTGACGGAGCCCTGCGGCAACTCCACCTTGTGTGTCCCA
43 I G L F C C R G C P A G H Y L K A P C T E P C G N S T C L V C P Q
601 AGACACCTTCTTGGCCTGGGAGAACCAACCAATAATTCTGAATGTGCCCGCTGCCAGGCGCTGTGATGAGCAGGCGCTCCAGGTGGCGCTGGAGAACTGTCA
76 D T F L A W E N H H N S E C A R C Q A C D E Q A S Q V A L E N C S
701 GCAGTGGCCGACCCGCTGTGGCTGTAGCCAGGCTGGTGTGGAGTGCAGGCAATGTGTGACAGCTTACCCCTTCTACTGCCAACCATGCC
109 A V A D T R C G C K P G W F V E C Q V S S S P F Y C Q P C L
801 TAGACTGCGGGCCCTGCACCGCCACACACGGCTACTCTGTTCCCGCAGAGATACTGACTGTGGGACCTGCCCTGGCTTCTATGAACATGGCGATGG
143 D C G A L H R H T R L L C S R R D T D C G T C L P G F Y E H G D G
901 CTGCGTGTCTGCCCGACGTAATTCCTAGCTGTCTGGGATGGAGGGAAGGCGCTGGGAGCAGGCGCTGGGGTGGGCGAGGTGCTGTGGTT
176 C V S C P T
1001 CAGGAATAGGAAGGGGATAGGAGGAGGAGCCCTTGGCCCTGTGATGGTGGGCCCACTTCAGGCAAACTTAGATGGCAAAAGAGCAATCTGGATCC
1101 GCCTTAGCCAGATACATAAGGGTATTGCTTTCAGCCAGCATTCCTCCCGCAGGATCCTAGCCAGATATTACAGATGATTGTCACTTACACAGA
1201 GAGTCACATTGATATAGCTTTAAACTTGGGCTGAAGGAGGTGAGCTGAGCTATGATCGTGCCACTGCACCTTCAGCCTGGGCAACAGAGCGAG
1301 ACCTATTAAATAAATAAATAATTAAATCTATTAAATAATTAAATAAATAAAGGGCTGAGAGTCAGGACTGTGCTGC
1401 TAGTTCTAGGGGATCTTGGGCAAGTGCAGAGAATTC

FIG. 1

J

seq 1000 1000 1000 1000 1000 1000 1000 1000 1000 1000
 from 1000 1000 1000 1000 1000 1000 1000 1000 1000 1000
 if 1000 1000 1000 1000 1000 1000 1000 1000 1000 1000
 then 1000 1000 1000 1000 1000 1000 1000 1000 1000 1000

hApo2LI	34	D	C	A	G	D	-	-	-	F	H	K	K	I	G	L	F	C	C	R	G	C	P	A	G	H	Y	L	K	A	P	C	T	E	P	C	G	N	S	T	C	L	-	-	-	-	-	-
hTNFR1	43	V	C	P	Q	G	K	-	-	Y	I	H	P	Q	N	N	S	I	C	C	T	K	C	H	K	G	T	Y	L	Y	N	D	C	P	G	P	G	Q	D	T	D	C	R	-	-	-	-	-
hTNFR2	39	T	C	R	L	R	E	-	-	Y	Y	D	Q	T	A	Q	M	C	C	S	K	C	S	P	G	Q	H	A	K	V	F	C	T	K	T	-	S	D	T	V	C	D	-	-	-	-	-	
hTNFR1p	42	T	C	R	D	Q	E	K	E	-	Y	Y	E	P	Q	H	R	I	C	C	S	R	C	P	P	G	T	Y	V	S	A	K	C	S	R	I	-	R	D	T	V	C	A	-	-	-	-	
hFAS/Apo1	48	N	L	E	G	L	-	-	-	-	H	H	D	G	Q	F	C	H	K	P	C	P	P	P	G	E	R	K	A	R	D	C	T	V	N	G	D	E	P	D	C	V	-	-	-	-	-	
hLINGFR	31	A	C	P	T	G	-	-	-	-	L	Y	T	H	S	G	E	C	C	K	A	C	N	L	G	E	G	V	A	Q	P	C	G	A	-	-	N	Q	T	V	C	E	-	-	-	-		
hCD40	25	A	C	R	E	K	-	-	-	-	Q	Y	L	I	N	S	Q	C	C	S	L	C	Q	P	G	Q	K	L	V	S	D	C	T	E	F	-	T	E	T	C	L	-	-	-	-	-		
hCD27	26	S	C	P	E	R	-	-	-	H	Y	W	A	Q	G	K	L	C	C	Q	M	C	E	P	G	T	F	L	V	K	D	C	D	Q	H	R	K	A	Q	C	D	-	-	-	-	-		
hCD30	28	T	C	H	G	N	P	S	H	-	Y	Y	D	K	A	V	R	R	C	C	Y	R	C	P	M	G	L	F	P	T	Q	Q	C	P	Q	R	-	-	P	T	D	C	R	K	-	-		
hOX40	30	H	C	V	G	D	T	-	-	-	Y	P	S	N	D	R	C	C	H	E	C	R	P	G	P	G	N	G	M	V	S	R	C	S	R	S	-	Q	N	T	V	C	R	-	-	-	-	

hApo2LI	72	V	C	P	Q	D	-	T	F	L	A	W	E	N	H	H	S	E	C	A	R	C	-	Q	A	C	D	E	Q	A	S	Q	V	A	L	E	N	C	S	A	V	A	D	T	R	C	G	-	-	-	-
hTNFR1	83	E	C	E	S	G	-	S	F	T	A	S	E	N	H	L	R	H	C	L	S	C	-	S	K	C	R	K	E	M	G	Q	V	E	I	S	S	C	T	V	D	R	D	T	V	C	G	-	-	-	-
hTNFR2	77	S	C	E	D	S	T	Y	T	Q	L	W	N	W	V	-	P	E	C	L	S	C	G	S	R	C	S	S	-	-	D	Q	V	E	T	Q	A	C	T	R	E	Q	N	R	I	C	T	-	-	-	
hTNFR1p	82	T	C	A	E	N	S	Y	N	E	H	W	N	Y	L	-	T	I	C	Q	L	C	-	R	P	C	D	P	V	M	G	L	E	E	I	A	P	C	T	S	K	R	K	T	Q	C	R	-	-	-	
hFAS/Apo1	84	P	C	Q	E	G	K	E	Y	T	D	K	A	H	F	S	S	K	C	R	R	C	-	R	L	C	D	E	G	H	G	L	E	V	E	I	N	C	T	R	T	Q	N	T	K	C	R	-	-		
hLINGFR	66	P	C	L	D	S	V	T	F	S	D	V	S	A	T	E	P	C	K	P	C	-	T	E	C	V	G	L	-	-	Q	S	M	S	A	P	C	V	E	A	D	D	A	V	C	R	-	-			
hCD40	61	P	C	G	E	S	E	F	L	D	T	W	N	R	E	-	T	H	C	H	Q	H	-	K	Y	C	D	P	N	L	G	L	R	V	Q	Q	K	G	T	S	E	T	D	T	I	C	T	-	-		
hCD27	64	P	C	I	P	G	V	S	F	S	P	D	H	H	T	R	P	H	C	E	S	C	-	R	H	C	N	S	G	L	L	V	R	-	-	N	C	T	I	T	A	N	A	E	C	A	-	-			
hCD30	68	Q	C	E	P	D	-	Y	Y	L	D	E	A	D	R	-	-	-	C	T	A	C	-	V	T	C	S	R	D	D	L	V	E	K	T	-	P	C	A	W	N	S	S	R	V	C	E	-			
hOX40	66	P	C	G	P	G	-	F	Y	N	D	V	S	S	K	P	-	-	C	K	P	C	-	T	W	C	N	L	R	S	G	S	E	R	K	Q	L	C	T	A	T	Q	D	T	V	C	R	-			

FIG. 2A

hApo2LI	116	C K P G	W F V E C Q V S Q C V S S S P F Y C	Q P C L D C G A L H R H T R L L C S R R D -	T D C G - T
hTNFR1	127	C R K N	Q Y R H Y W S E N L - - - - F Q C	F N C S L C L N G - - T V H L S C Q E K Q N T	V C - - T
hTNFR2	120	C R P G	W Y C A L S K Q E G C - - - - R L C	A P L R K C R P G - F G V A R P G T E T S D V V	C K - P
hTNFR1p	126	C Q P G	M F C A A W A L E C - - - - T H C	E L L S D C P P G T E A E L K D E V G K G N N H C V -	P
hFAS/Apo1	129	C K P N	F - - C N S T V C - - - - E H C	D P C T K C E H G I - - - I K E C T L T S N T	K C K -
hLNGFR	109	C A Y G	Y Y Q D E T T - - - - - G R C	E A C R V C E A G S G L - V F S C Q D K Q N T	V C E - E
hCD40	105	C E E G	W H C T S E A C - - - - - E S C	V L H R S C S P G F G - V K Q I A T G V S D T	I C E - P
hCD27	106	C R N G	W Q C R D K E C - - - - - T E C	D P L P N P S L T A R S S Q A L S P H P Q P T	H L P -
hCD30	108	- C R P G	M F C S T S A V N S C - - - - A R C	F F H S V C P A G M I V K F P G T A Q K -	N T V C E -
hOX40	109	- C R A G	T Q P L D S Y K P G - - - - - V D C A -	- - - - -	- - - - -

FIG. 2B

1081 GGGCCCGCAG CTCTACGACG TGATGGACGC GGTCCACGCG CCGCGCTGGA AGGAGTTCGT
332 G P Q L Y D V M D A V P A R R W K E F V

1141 GCGCAGCTG GGGCTGCGG AGGCAGAGAT CGAAGCCGTG GAGTGGAGA TCGGCCGCTT
352 R T L G L R E A E I E A V E V E I G R F

1201	CCGAGACCA	CAGTACG	A	TGCTCAAG	CG	CTGGCGCC	AG	CAGCAGCC	CG	CGGGCCTCGG
372	R D Q	Q Y E	M	L K R	W	R Q	Q Q	P A	G L	G

1261 AGCCGTTTAC GCGGCCCTGG AGCGCATGGG GCTGGACGGC TCGGTGGAAG ACTTGCGCAG
392 A V Y A A L E R M G L D G C V E D L R S

1321 CCGCCTGCAG CGCGGCCCGT GACACGGCGC CCACTTGCCA CCTAGGCGCT CTGGTGCCCC
412 R L Q R G P

1381 TTGCAGAAGC CCTAAGTACG GTTACTTATG CGGTAGACA TTTTATGTCA CTTATTAAGC

1441 CGCTGGCAG GCCCTGCGTA GCAGCACCAG CCGGCCCCAC CCCTGCTCGC CCCTATCGCT

1501 CCAGCCAAGG CGAAGAAGCA CGAACGAATG TCGAGAGGGG GTGAAGACAT TTCTCAACTT

1561 CTCGGCCGGA GTTTGGCTGA GATCGCGGTA TTAAATCTGT GAAAGAAAC AAAAAAAAAA

1621 AAAAAAAAAA AAAA

FIG. 4C

more than 1000 times in the genome of the human
cell. It is a very common mutation in the human
genome and is found in all human cells.

541 ACGGCTACTC TGTTCCCGCA GAGATACTGA CTGTGGGACC TGCCCTGCCCTG GCTTCTATGA
152 R L L C S R R D T D C G T C L P G F Y E

601 ACATGGCGAT GGCTGGGTGT CCTGCCCCAC GAGCACCCCTG GGGAGCTGTC CAGAGCGCTG
172 H G D G C V S C P T S T L G S C P E R C

661 TGCCGCTGTC TGTGGCTGGA GGCAGATGTT CTGGGTCCAG GTGCTCCTGG CTGGCCTTGT
192 A A V C G W R O M F W V O V L L A G L Y

721 GGTCGCCCTC CTGCTTGGG CCACCCCTGAC CTACACATAC CGCCTGCT GGCCTCACAA
212 V P L L L G A T L T Y T Y R H C W P H K

781 GCCCCTGGTT ACTGCAGATG AAGCTGGGAT GGAGGCTCTG ACCCACCAC CGGCCACCCA
232 P L V T [A] D E A G M E A L T P P P A T H

841 TCTGTCACCC TTGGACAGCG CCCACACCCT TCTAGCACCT CCTGACAGCA GTGAGAAGAT
252 L S P L D S A H T L L A P P D S S E K I

901 CTGCACCGTC CAGTTGGTGG GTAACAGCTG GACCCCTGGC TACCCCGAGA CCCAGGAGGC
272 C T V Q L V G N S W T P G Y P E T Q E A

961 GCTCTGCCCG CAGGTGACAT GGTCTGGGA CCAGTTGCCC AGCAGAGCTC TTGGCCCCGC
292 L C P Q V T W S W D Q L P S R A L G P A

1021 TGCTGCGCCC ACACTCTCGC CAGAGTCCCC AGCCGGCTCG CCAGCCATGA TGCTGCAGCC
312 A A P T L S P E S P A G S P A M M L Q P

FIG. 4B

1 CGGGCCCTGC GGGCGCGGGG CTGAAGGCGG AACACGACG GGCAGAGAGC ACGGAGCCGG
61 GAAGCCCTG GCGCCCGTC GGAGGGCTAT GGAGCAGCGG CCGCGGGGCT GCGCGGCGGT
1 M F O R P R G C A A V
121 GCGGCGGCG CTCCTCCTGG TGCTGCTGGG GGCCCGGGCC CAGGCGGCA CTCGTAGCCC
12 A A A L L L V L L G A R A Q G G T R S P
181 CAGGTGTGAC TGTGCCGGTG ACTTCCACAA GAAGATTGGT CTGTTTGTG GCAGAGGCTG
32 R C D C A G D F H K K I G L F C C R G C
241 CCCAGCGGG CACTACCTGA AGGCCCTTG CACGGAGCCC TCGGCAACT CCACCTGCCT
52 P A G H Y L K A P C T E P C G N S T C L
301 TGTGTGTCC CAAGACACCT TCTTGGCCTG GGAGAACAC CATAATTCTG AATGTGCCC
72 V C P Q D T F L A W E N H H N S E C A R
361 CTGCCAGGCC TGTGATGAGC AGGCCTCCCA AGTGGGCTG GAGAACTGTT CAGCAGTGGC
92 C Q A C D E Q A S Q V A L E N C S A V A
421 CGACACCCGC TGTGGCTGTA AGCCAGGCTG GTTGTGGAG TGCCAGGTCA GCCAATGTGT
112 D T R C G C K P G W F V E C Q V S Q C V
481 CAGCAGTTCA CCCTTCTACT GCCAACCATG CCTAGACTGC GGGGCCCTGC ACCGCCACAC
132 S S S P F Y C Q P C L D C G A L H R H T

FIG. 4A



Apo3	1	M E Q R P R G C A A V A A A L L V L L G A R A Q G G T R S P R - - - - -
TNFR1	1	M G L S T V P D L L L P L - V L L E L L V G I Y P S G V I G L V P H L G D R E K R D S V
Fas/Apo1	1	M L G I W T L L P L V L T S V A R L S S K S V N A Q V T D I N S K G L E L R K T V T T V
Apo3	33	C D C A G D F H K K I G L F C C R G C P A G H Y L K A P C T E P C G N S T C L V
TNFR1	44	C P Q G K Y I H P Q N S I C C T K C H K G T Y L Y N D C P G P G Q D T D C R E
Fas/Apo1	45	E T Q N L E G L H H D G Q F C H K P C P P G E R K A R D C T V N G D E P D C V P
Apo3	73	C P Q D T F L A W E N H H N S E C A R C Q A C D E Q A S Q V A L E N C S A V A D T R C G
TNFR1	85	C E S G S F T A S E N H L R H - C L S C S K C R K E M G Q V E I S S C T V D R D T V C G
Fas/Apo1	85	C Q E G K E Y T D K A H F S S K C R C R L C D E G H G L E V E I N C T R T Q N T K C R
Apo3	117	C K P G W F V E C Q V S Q C V S S S P F Y C Q P C L D C G A L H R H T R L L C S R R D - T D C G T
TNFR1	127	C R K N Q Y R H Y W S E N L F Q - - - - - C F N C S L C L N G T V H L S - - C Q E K Q N T V C T -
Fas/Apo1	129	C K P N F F - - C N S T V C E H - - - - - C D P C T K C E H G I I K E - - - C T L T S N T K C K E
Apo3	165	C L P G F Y E H G D G C V S C P T S T L G S C P - - E R C A A V C G W
TNFR1	168	C H A G F F L R E N E C V S C S - - - - - N C K K S L E C T K L C L P

Apo3	338	VMDA	V	P	A	R	R	W	K	E	F	V	R	T	L	G	L	R	E	A	E	I	E	A	V	E	I	G	R	-	-	F	R	D	Q	Q	Y	E			
TNFR1	333	VVEN	V	P	P	L	R	W	K	E	F	V	R	R	L	G	L	S	D	H	E	I	D	R	L	E	L	Q	N	G	R	-	C	L	R	E	A	Q	Y	S	
Fas/Apo1	220	IAGV	M	T	L	S	Q	V	K	G	F	V	R	K	N	G	V	N	E	A	K	I	D	E	I	K	N	D	N	V	Q	D	T	A	E	Q	K	V	-	Q	
FADD	104	ICDN	V	G	K	-	D	W	R	R	L	A	R	Q	L	K	V	S	D	T	K	I	D	S	I	E	D	R	Y	P	R	N	-	L	T	E	R	V	R	E	
TRADD	211	NRP	L	S	L	K	-	D	Q	Q	T	F	A	R	S	V	G	L	K	W	R	K	V	G	R	-	S	L	Q	R	G	C	R	A	L	R	D	P	A	L	D
RIP	291	IREN	L	G	K	-	H	W	K	N	C	A	R	K	L	G	F	T	Q	S	A	I	D	E	I	D	H	D	Y	E	R	D	G	L	K	E	K	V	Y	Q	
Reaper	1							M	A	V	A	F	Y	I	P	D	Q	A	T	L	R	E	A	E	Q	K	E	Q	I	L	R	-	L	R	E	S	Q	W	R		

E/G. 6

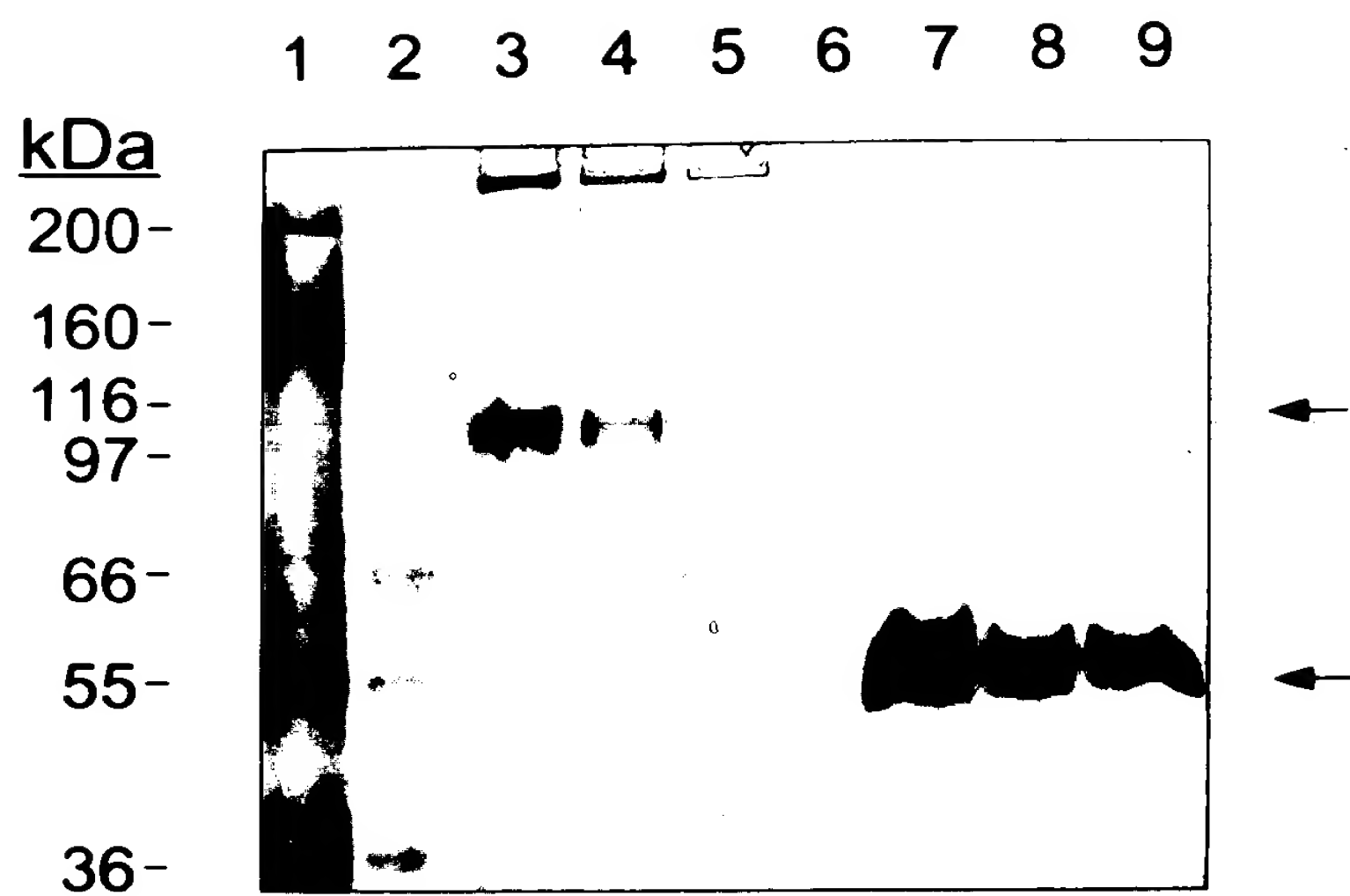


FIG. 3

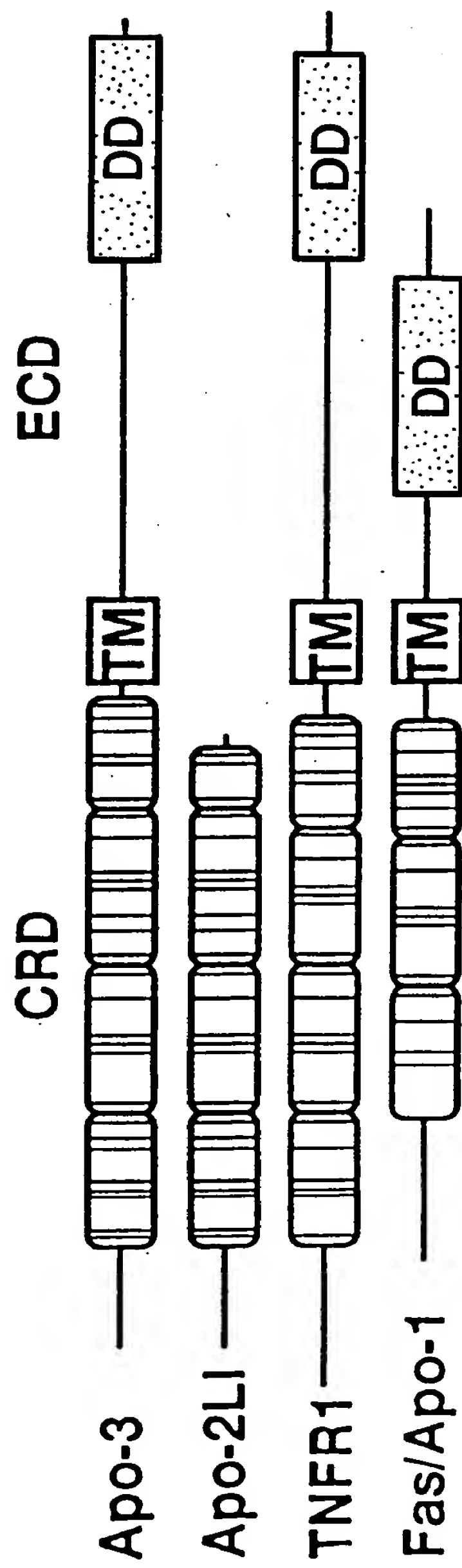
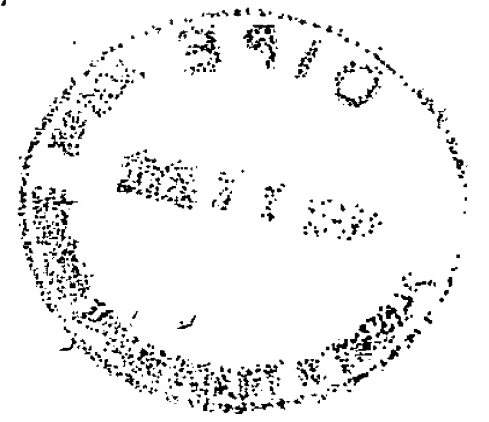
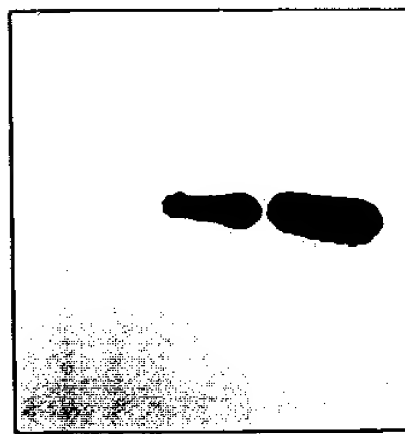


FIG. 7



Transfection

pRK5
TNFR1
Apo-3



◀ **Phospho-C-Jun**

FIG. 11

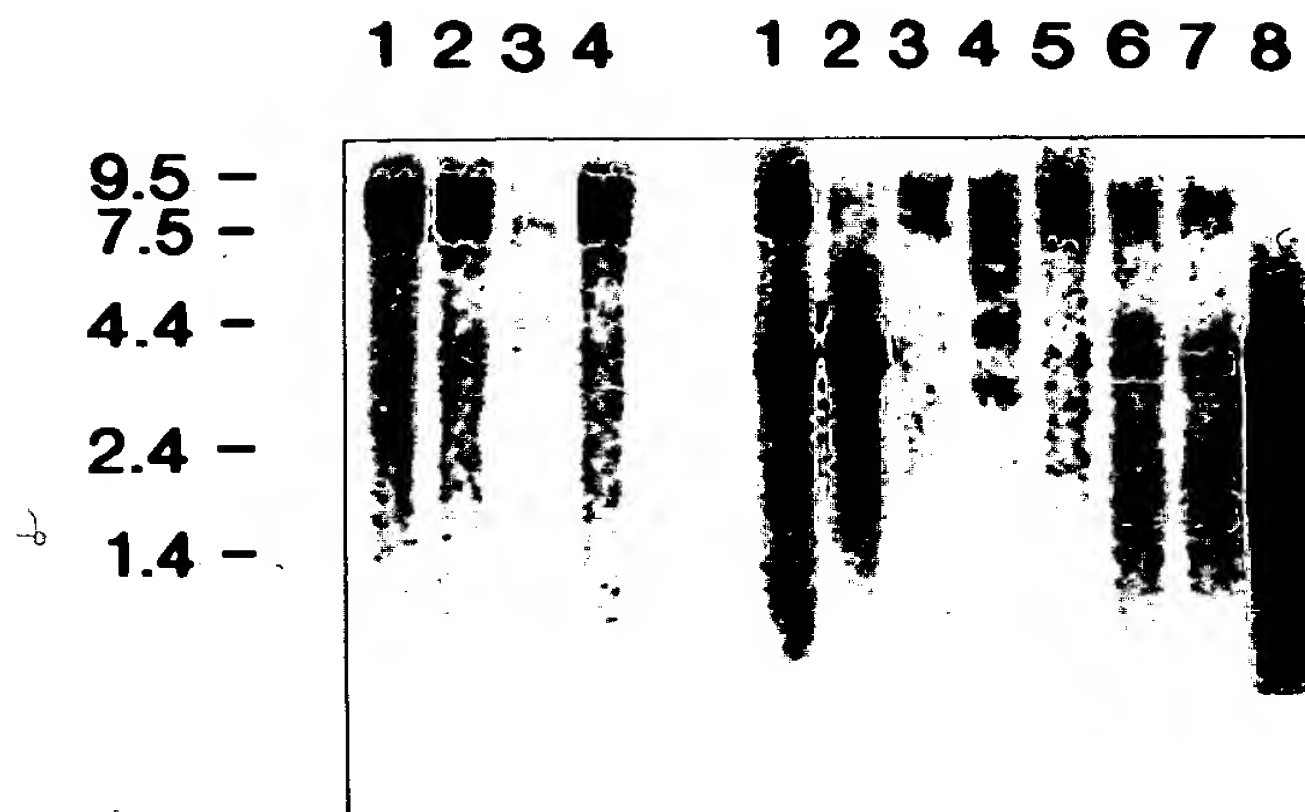


FIG. 12

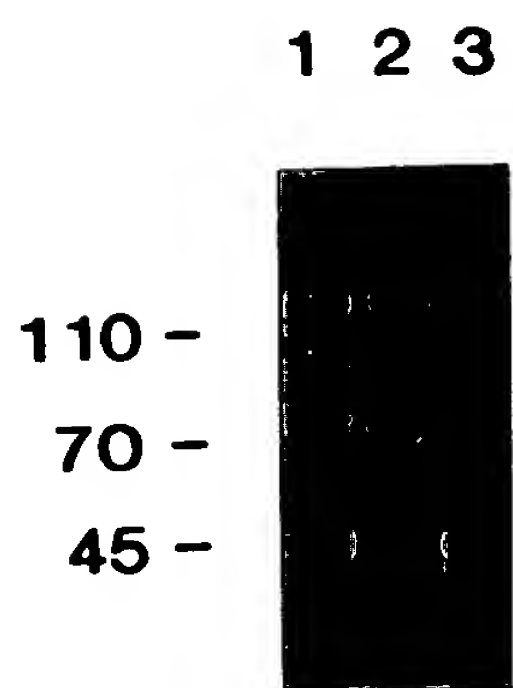


FIG. 8

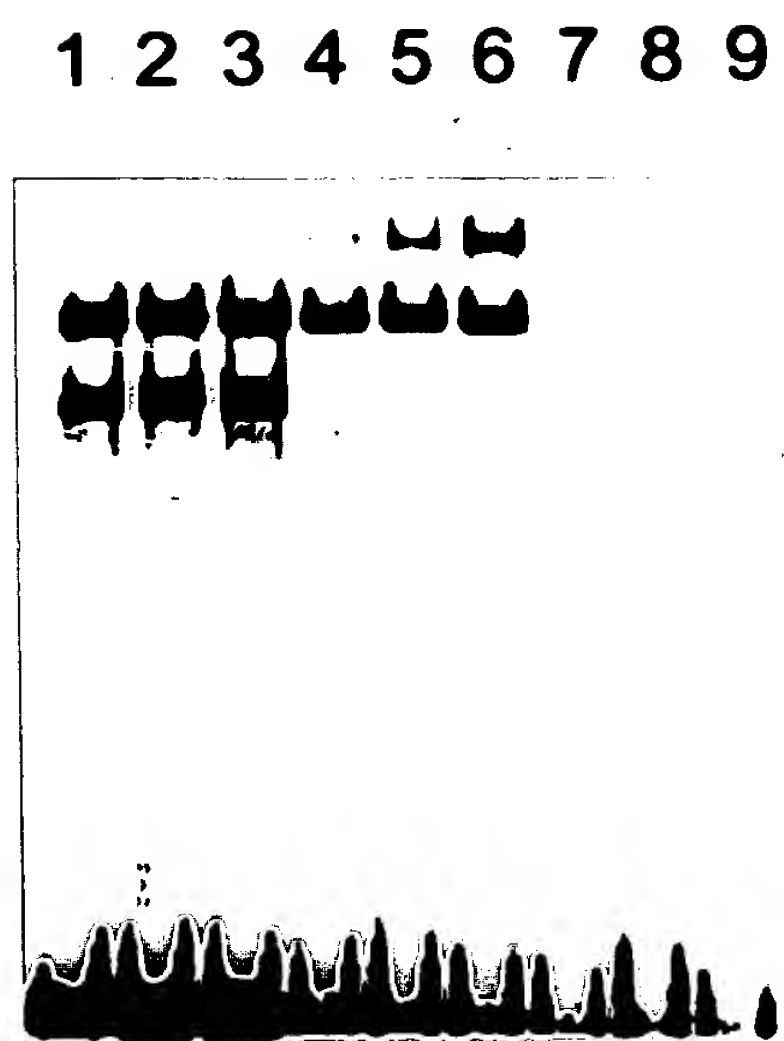


FIG. 10

FIG. 9A



FIG. 9B



FIG. 9C

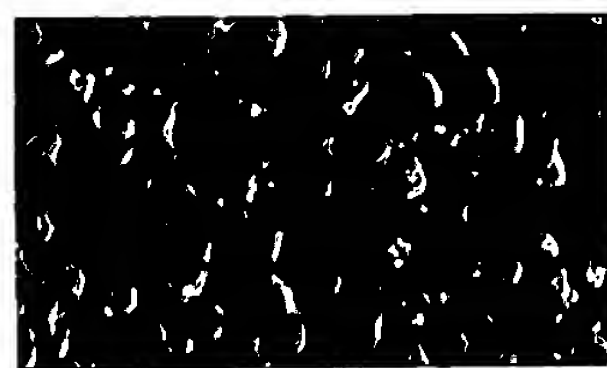


FIG. 9D

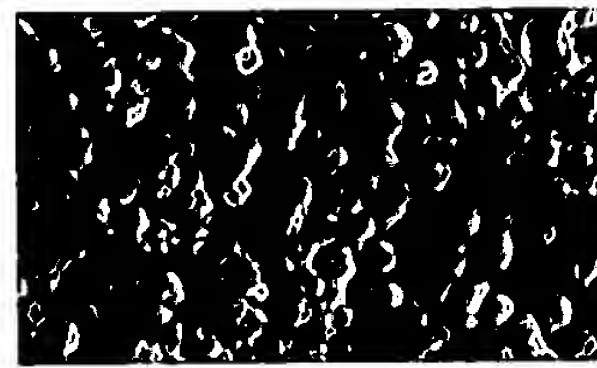


FIG. 9E



FIG. 9F

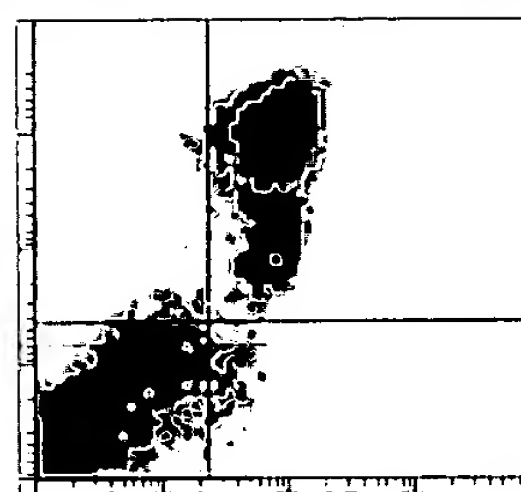


FIG. 9G

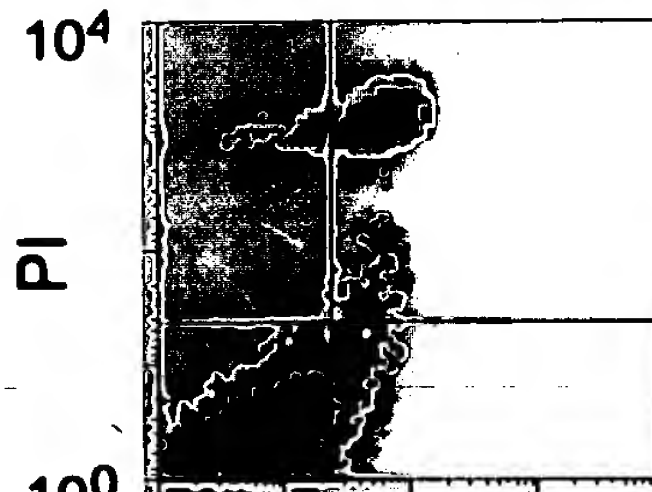


FIG. 9H

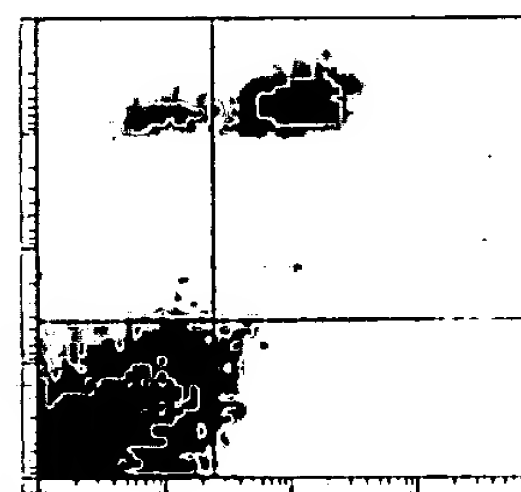


FIG. 9I

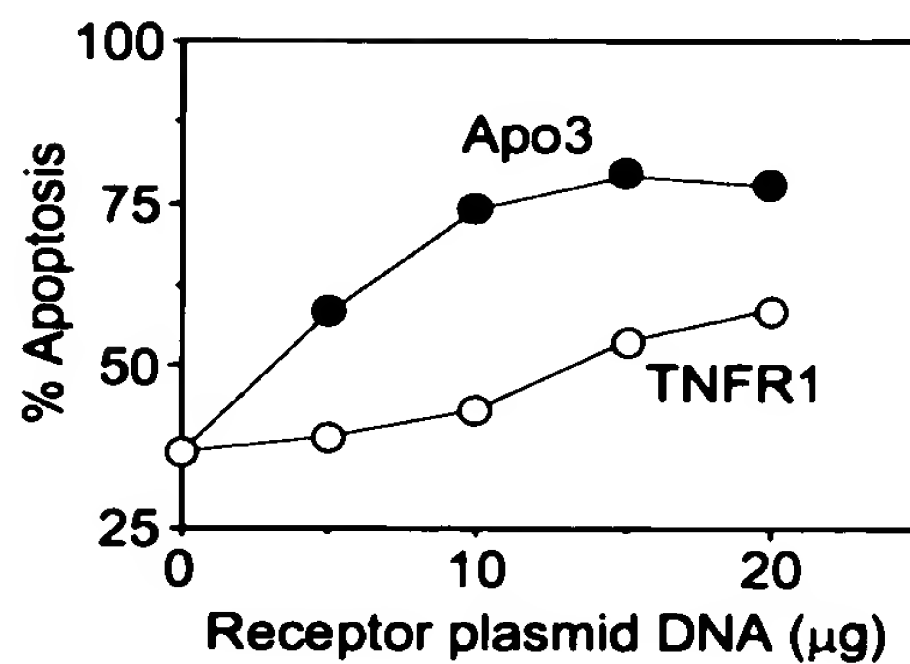


FIG. 9J

